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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/647,695	04/06/2001	Sean Farmer	19374-502	1128

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EXAMINER	
DAVIS, RUTH A	

ART UNIT	PAPER NUMBER
1651	19

DATE MAILED: 11/03/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/647,695	FARMER ET AL.	
	Examiner	Art Unit	
	Ruth A. Davis	1651	

-- The MAILING DATE of this c mmunication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 July 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4 and 8-77* is/are pending in the application.

4a) Of the above claim(s) *31-76* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4,8-30,77* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicant's request for continued examination and amendment filed July 24, 2003 has been received and entered into the case. Claims 31 – 76 are withdrawn from consideration; claims 1, 4, 8 – 30 and 77 have been considered on the merits. All arguments have been fully considered.

Claim Objections

1. Claim objections have been withdrawn due to amendment.

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 1, 4, 8 – 30 and 77 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Paul in view of Fukushima, Bova and Mandeville.

Applicant claims a method for decreasing serum cholesterol and increasing serum HDL comprising orally administering an effective amount of a composition comprising Bacillus coagulans and a therapeutic composition comprising an effective amount of a cholesterol reducing agent and a bifidogenic oligosaccharide. The composition contains 10^5 – 10^10 viable bacterium/gram composition. Administration is oral at 0.1 – 5 grams/day, 10^8 – 10^10 viable bacterium per day or 5 X 10^8 – 10^9 viable bacterium/day. Administration is 10 mg – 20 or 150 mg – 5 grams of bifidogenic oligosaccharide per day. The bifidogenic oligosaccharide is selected from fructo-oligosaccharide, gluco-oligosaccharide or trisaccharide raffinose wherein fructose-oligosaccharide comprises polymers of fructose and glucose with a chain length of about 4 – 100 sugar units. The composition comprises 10 mg – 1 gram or 100 – 500 mg of bifidogenic oligosaccharide per gram composition. The cholesterol reducing agent is one of a statin, a bile sequestering compound, a fiber product capable of binding cholesterol, niacin or aspirin. The statin is one of cervastatin, fluvastatin, lovastain, pravastatin or simvastatin and is administered at 10 – 80 mg of statin per day, The bile sequestering agent is one of colestipol or cholestyramine and is administeres at 1 – 20 grams per day. The fiber is one of gemfibrozil, fenofibrate, psyllium bran, glucomannan or Jerusalem artichoke flour and is administeres at 500 mg – 50 grams of fiber per day. The composition further comprises a cholic acid complexation agent selected from a metal salt of calcium, chromium copper, iodine, iron, magnesium, manganese, potassium, sodium or zinc. The metal salt is calcium citrate, potassium gluconate, magnesium citrate or chromium picollinate. The composition further comprises a food

substance, flavoring, vitamin or mineral. Further, the patient is at risk for atherosclerosis, arterial sclerosis, myocardial infarction, heart attack, diabetes, coronary heart disease, angina pectoris or unstable angina. Finally, Applicant claims a method for decreasing serum cholesterol and increasing serum HDL comprising orally administering an effective amount of a composition comprising Sporolactobacillus, or S. P44, and a therapeutic composition selected from a cholesterol reducing agent or a bifidogenic oligosaccharide.

Paul teaches oral administration of a composition comprising dietary fiber (cholesterol reducing agent), fructooligosaccharide (FOS), and a beneficial human intestinal microorganism (lactic acid bacteria) wherein the microorganism is Lactobacillus or Bifidobacteria (abstract). Specific lactic acid microorganisms are disclosed to include L. acidophilus, L. casei, L. salivarius, L. brevis, L. plantarum, B. adolescentis, B. infantis, B. longum and B. bifidum (col.4 line 20-30).

The ingredients are combined with juice or water and are taken in dosages of about 20 – 400 mg/kg body weight (col.14 line 5-10). Paul discloses compositions such as this have beneficial effects on cholesterol metabolism resulting in decreased serum cholesterol and increased HDL to LDL ratio (col.2 line 35-40). Specifically, FOS is disclosed to reduce serum cholesterol, improve HDL/LDL ratios and increase bifidobacterium populations (col.6 line 55-68).

Although Paul does not specifically teach administering the composition in a method to decrease serum cholesterol and increase serum HDL, the reference does teach these effects. Furthermore, by administering the composition of Paul, it is inherent that serum cholesterol

decreased and serum HDL increased. Moreover, by practicing the method of Paul, one in the art would inherently be decreasing serum cholesterol and increasing serum HDL.

Paul does not teach the specific amounts of viable microorganisms of bacterium or bifidogenic oligosaccharide per gram of composition or the administration dosages as claimed by applicant. However, it would have been obvious to one of ordinary skill in the art to optimize volumes of ingredients and effective amounts of bacterium because it was routine practice in the art at the time of the invention. At the time of the invention, one of ordinary skill in the art would have been motivated by Paul to optimize the effective amounts to reduce serum cholesterol and increase serum HDL because of these disclosed known actions of the composition. Moreover, at the time of the invention, one of ordinary skill in the art would have been motivated by Paul and conventional practice to optimize administration dosages and volumes of ingredients with a reasonable expectation of success to reduce serum cholesterol and increase serum HDL.

Paul does not teach the fructooligosaccharide with a chain length of 4 – 100 sugar units. However, at the time of the invention, it would have been obvious to one of ordinary skill in the art to substitute or optimize the size of fructooligosaccharide to enhance a desired effect because it was routine practice in the art at the time of the invention. Moreover, at the time of the invention, one of ordinary skill in the art would have been motivated by conventional practice to optimize the size of the fructooligosaccharide in the method of Paul, with a reasonable expectation of success for decreasing serum cholesterol and increasing serum HDL.

Paul does not teach Jerusalem artichoke flour as the fiber source. However, Paul does teach inulin as the fiber source (abstract). Specifically, Paul teaches Jerusalem artichoke is a rich

source of inulin (fiber) wherein Bifidobacterium uses it as an energy source (col. 6 line 5-20). At the time of the invention, one of ordinary skill in the art would have been motivated to use Jerusalem artichoke flour because of the fiber (inulin) content contained in Jerusalem artichoke as taught by Paul. One of ordinary skill in the art would have been further motivated to use Jerusalem artichoke flour because it was known to be a source of energy for Bifidobacterium as disclosed by Paul.

Paul does not teach the method wherein the patient is at risk for atherosclerosis, arterial sclerosis, myocardial infarction, heart attack, diabetes, coronary heart disease, angina pectoris or unstable angina. However, because of the disclosed beneficial effects on serum cholesterol and LDL/HDL ratios, it would have been obvious to one of ordinary skill in the art to practice the method of Paul on patients at risk for the aforementioned conditions because high cholesterol was a known symptom/indicator of each of the conditions. Moreover, at the time of the invention, one of ordinary skill in the art would have been motivated to practice the method of Paul on "at risk patients" with a reasonable expectation for success because of the disclosed benefits of reduced serum cholesterol and improved LDL/HDL ratios.

Paul does not teach the method wherein Bacillus species are used. However, at the time of the invention, it would have been obvious to one of ordinary skill in the art to utilize a Bacillus in the methods of Paul because Fukushima teaches the effects of a probiotic composed of Bacillus include reduced serum cholesterol and increased serum HDL (abstract). Although Fukushima does not teach specific species of Bacillus, the reference does teach the effect is achieved with the genus. Therefore, at the time of the invention, it would have been obvious to one of ordinary skill in the art to utilize any Bacillus as they were known to have the claimed

effect. Moreover, at the time of the invention, one of ordinary skill in the art would have been motivated by Fukushima to use a Bacillus in the methods of Paul with a reasonable expectation for success of decreasing serum cholesterol and increasing serum HDL because of the disclosed properties of Bacillus specifically achieving the claimed effect.

Paul does not teach the method wherein therapeutic agents include statins, cervastatin, flucastatin, lovastatin, pravastatin or simvastatin; bile sequestering agents, colestipol or cholestyramine; fiber sources gemfibrozil or fenofibrate; niacin or aspirin wherein they are administered in amounts as claimed by applicant. However, at the time of the invention, one of ordinary skill in the art would have been motivated to include any of the aforementioned agents in the composition and method of Paul because Bova teaches each of these are known to lower serum cholesterol (p.1, paragraphs 0006 – p.2 paragraph 0009). Bova teaches numerous methods for reducing serum cholesterol and increasing HDL cholesterol levels have been proposed to include administration of hypolipidemic agents, or lipid altering agents (p.1 paragraph 0006). Specifically, niacin and the named statins are disclosed to reduce total serum cholesterol and increase serum HDL cholesterol (p.2 paragraph 0010, 0017) while bile sequestering agents are disclosed to be a first choice for treating hypercholesterolemia due to their efficacy and proved usefulness (p.3 paragraph 0020). Furthermore, Bova teaches administration of statins in dosages between 10 – 80 mg, 5 – 80 mg and 20 – 80 mg (p.4 paragraph 0033). Therefore, at the time of the invention, one of ordinary skill in the art would have been motivated by Bova to include any of the above mentioned agents in the method of Paul, with a reasonable expectation of success for decreasing serum cholesterol and increasing

serum HDL because they were well known in the art for reducing cholesterol and increasing HDL as demonstrated by the references cited above.

The above references do not teach specific volumes of bile sequestering agents or fiber. However, at the time of the invention, it would have been obvious to one of ordinary skill in the art to optimize dosages of effective ingredients because it was routine practice in the art at the time of the invention. Moreover, at the time of the invention, one of ordinary skill in the art would have been motivated by conventional practice to optimize dosages of effective ingredients with a reasonable expectation of success for decreasing serum cholesterol and increasing serum HDL.

Paul does not teach the method further comprising administering a cholic acid complexation agent. However, at the time of the invention, one of ordinary skill in the art would have been motivated to include a cholic acid complexation (or sequestering, chelating) agent because Mandeville teaches that it is advantageous to sequester primary bile acids to significantly increase the reduction of serum lipid levels (col.1 line 55-65). At the time of the invention, it was known in the art that cholic acid is a primary bile acid and that sorption of bile acids is related to decreasing serum cholesterol (US 5427777 col.2 line 25-35). Although the reference does not teach the specific cholic acid complexation (sequestering) agents claimed by applicant, it would have been obvious to one of ordinary skill in the art to use any complexing agent as they were known in the art at the time of the invention. Moreover, at the time of the invention, one of ordinary skill in the art would have been motivated by Mandeville to include a cholic acid complexation (sequestering) agent in the method of Paul with a reasonable

expectation of success for reducing serum cholesterol because of the cholesterol/lipid reducing effects as demonstrated by Mandeville.

Applicant argues that Fukushima only teaches 3 Bacillus species, not the entire genus. Applicant further argues that while several lactic acid bacteria are taught, Fukushima does not teach Bacillus coagulans.

However, these arguments fail to persuade because the references clearly demonstrate that various lactic acid bacteria were well known to reduce serum cholesterol levels and increase serum HDL. Although the references do not specifically name Bacillus coagulans, one of ordinary skill in the art would certainly have been motivated by the cited references to use any known lactic acid bacteria in the composition and methods of Paul with a reasonable expectation for successfully decreasing serum cholesterol and increasing serum HDL. Absence of evidence regarding any unexpected advantage or benefit using the claimed bacteria, the claims remain obvious for these reasons and those made above.

Conclusion

1. This is an RCE of applicant's earlier Application No. 09/947,695. All claims are drawn to the same invention claimed in the earlier application and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the earlier application. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action in

this case. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no, however, event will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ruth A. Davis whose telephone number is 703-308-6310. The examiner can normally be reached on M-H (7:00-4:30); altn. F (7:00-3:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 703-308-0196. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Ruth A. Davis; rad
October 28, 2003

LEON B. LANKFORD, JR.
PRIMARY EXAMINER